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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/555,971	11/14/2000	Ivo Glynne Gut	147-201P	8231

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EXAMINER	
LU, FRANK WEI MIN	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 10/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/555,971	GUT ET AL.	
	Examiner	Art Unit	
	Frank W Lu	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 August 2004* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *11-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 14-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on *06 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8/2004* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Response to Amendment

1. Applicant's response to the office action filed on August 5, 2004 has been entered. The claims pending in this application are claims 1-20 wherein claims 11-13 have been withdrawn due to species election. Rejection and/or objection not reiterated from the previous office action are hereby withdrawn in view of the amendment filed on August 5, 2004.

Specification

2. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. For example, see description for Figure 4 in page 14 (see amendment filed on October 6, 2003). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. Note that applicant does not address this issue.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-10 and 14-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Claim 1 recites the limitation "said nucleotide molecules" in last line of the claim. There is insufficient antecedent basis for this limitation in the claim since there is no "nucleotide molecules" in claim 1 and claim 1 only has nucleic acid molecules. Please clarify.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 1-3, 6-10, 14, 16, 17, 19, and 20 are rejected under 35 U.S.C. 102(e) as being anticipated by Ness *et al.*, (US Patent No. 6,613,508 B1, filed on July 22, 1997).

Ness *et al.*, teach methods and compositions for analyzing nucleic acid molecules utilizing sizing techniques.

Regarding claim 1, Ness *et al.*, teach a method for genotyping a selected organism, comprising the steps of (a) combining tagged nucleic acid molecules with a selected target molecule under conditions and for a time sufficient to permit hybridization of the tagged molecules to the target molecule, wherein a tag is correlative with a particular fragment and is detected by non-fluorescent spectrometry or potentiometry, (b) separating the tagged fragments by sequential length or by size; (c) cleaving the tag from the tagged fragment, and (d) detecting the tag by non-fluorescent spectrometry or potentiometry, and therefrom determining the genotype of the organism (see columns 2-4 and 54). Since Ness *et al.*, teach combining tagged

nucleic acid molecules with a selected target molecule under conditions and for a time sufficient to permit hybridization of the tagged molecules to the target molecule and separating the tagged nucleic acid molecules by sequential length or by size (see columns 2, 3, and 54), the tagged nucleic acid molecules taught by Ness *et al.*, are with different mass. Therefore, Ness *et al.*, disclose hybridization of nucleic acid molecules to a set of probes of different nucleobase sequences, wherein each probe has a mass that differs from the one of all the other probes as recited in step (a) of claim 1. Since Ness *et al.*, teach separating the tagged nucleic acid molecules by sequential length or separating the target molecules, hybridized tagged probes, unhybridized probes or target molecules, probe:target hybrids, or tagged nucleic acid probes or molecules from other molecules utilizing methods which discriminate between the size of molecules such as HPLC or size exclusion chromatography (see columns 2-4 and 54) and it is known that HPLC or size exclusion chromatography is performed in a solvent, Ness *et al.*, disclose separation of the probes that are not hybridized and detachment of the probes that are hybridized in a solvent as recited in steps (b) and (c) of claim 1. Since Ness *et al.*, teach cleaving the tag from the separated tagged nucleic acid molecules and detecting the tag by non-fluorescent spectrometry or potentiometry (see columns 2-4 and 54) such as electrospray ionization mass spectrometry (see column 3, last paragraph), Ness *et al.*, disclose analysis of the probes that are detached from step (c) by means of electrospray mass spectrometry as recited in step (d) of claim 1. Since, as shown above, Ness *et al.*, teach steps (a) to (d) for genotyping a selected organism, Ness *et al.*, disclose detecting the nucleotide sequence in the nucleic acid molecules by means of the probes hybridized to the nucleotide sequence as recited in step (e) of claim 1.

Regarding claim 2, Ness *et al.*, teach that the nucleic acid molecules (ie., a DNA population which is covalently immobilized to the solid support and generated from mRNA) are immobilized at a surface of a support before step (a) as recited in claim 2 (see column 54, lines 30-67).

Regarding claim 3, since Ness *et al.*, teach that the amines on the polymers of the solid support (ie., glass surface) are used to covalently immobilize oligonucleotides (see column 55, lines 9-67) and it is known that glass surface is a surface of the supports with a silicate or silane, Ness *et al.*, disclose that the immobilization of the nucleic acid molecules at the surface is carried out via NH_2 as recited in claim 3.

Regarding claims 6-8, since Ness *et al.*, teach that each of nucleic acid probes is labeled with a cleavable mass spectrometry tag (see column 54, lines 30-67) wherein the tag carries a positive or negative charge (see column 16, lines 20-60), Ness *et al.*, disclose that the probes are nucleic acids having a mass tag as recited in claim 6, the mass tag is also a charge tag as recited in claim 7, and the nucleic acids have a charge tag as recited in claim 8.

Regarding claims 9 and 10, since nucleic acid defined by Ness *et al.*, can be a nucleic acid analog such as PNA (see column 10, last paragraph), Ness *et al.*, disclose that the probes are modified nucleic acid molecules wherein the modified nucleic acid molecules are PNAS as recited in claims 9 and 10.

Regarding claim 14, since Ness *et al.*, teach that nucleic acids are "amine-modified" in that they have been modified to contain a primary amine at the 5'-end of the nucleic acids (see column 94) and the "amine-modified" base is capable of cleaving by at least one chemical method, Ness *et al.*, disclose that the probes have at least one modification (ie., at the 5'-end of

the nucleic acid) in a defined position which allows for the cleavage of the probes as recited in claim 14.

Regarding claim 16, since the tagged nucleic acid molecules are more than one probes that are from an oligonucelotide combinatorial library generated by combinatorial chemistry (see columns 29 and 30) and each probe has a mass that differs from the one of all the other probes (see above rejection on claim 1), Ness *et al.*, disclose that the probes are generated as partial libraries having different mass as recited in claim 16.

Regarding claim 17, since, after step (a) of claim 1, hybridized probes are indirectly immobilized on the surface of the support (see column 54, lines 30-67), Ness *et al.*, disclose that the positions of the probes on the support allow for an allocation to the nucleic acid molecules hybridizing thereto as recited in claim 17.

Regarding claim 19, Ness *et al.*, teach a method for genotyping a selected organism, comprising the steps of (a) combining tagged nucleic acid molecules with a selected target molecule under conditions and for a time sufficient to permit hybridization of the tagged molecules to the target molecule, wherein a tag is correlative with a particular fragment and is detected by non-fluorescent spectrometry or potentiometry, (b) separating the tagged fragments by sequential length or by size, (c) cleaving the tag from the tagged fragment, and (d) detecting the tag by non-fluorescent spectrometry or potentiometry, and therefrom determining the genotype of the organism (see columns 2-4 and 54). Since Ness *et al.*, teach combining tagged nucleic acid molecules with a selected target molecule under conditions and for a time sufficient to permit hybridization of the tagged molecules to the target molecule and separating the tagged nucleic acid molecules by sequential length by size (see columns 2, 3, and 54) and the tagged

nucleic acid molecules are more than one probes that are from an oligonucelotide combinatorial library generated by combinatorial chemistry (see columns 29 and 30), the tagged nucleic acid molecules taught by Ness *et al.*, are partial libraries having different mass. Therefore, Ness *et al.*, disclose hybridization of nucleic acid molecules to a set of probes of different nucleobase sequences, wherein each probe has a mass that differs from the one of all the other probes and wherein the probes are generated as partial libraries having different mass as recited in step (a) of claim 19. Since Ness *et al.*, teach separating the tagged nucleic acid molecules by sequential length or separating the target molecules, hybridized tagged probes, unhybridized probes or target molecules, probe:target hybrids, or tagged nucleic acid probes or molecules from other molecules utilizing methods which discriminate between the size of molecules such as HPLC or size exclusion chromatography (see columns 2-4 and 54) and it is known that HPLC or size exclusion chromatography is performed in a solvent, Ness *et al.*, disclose separation of the probes that are not hybridized and detachment of the probes that are hybridized in a solvent as recited in steps (b) and (c) of claim 19. Since Ness *et al.*, teach cleaving the tag from the separated tagged nucleic acid molecule and detecting the tag by non-fluorescent spectrometry or potentiometry (see columns 2-4 and 54) such as electrospray ionization mass spectrometry (see column 3, last paragraph), Ness *et al.*, disclose analysis of the probes that are detached from step (c) by means of electrospray mass spectrometry as recited in step (d) of claim 19. Since, as shown above, Ness *et al.*, teach steps (a) to (d), Ness *et al.*, disclose detecting the nucleotide sequence in the nucleic acid molecules by means of the probes hybridized to the nucleotide sequence as recited in step (e) of claim 19.

Regarding claim 20, Ness *et al.*, teach a method for genotyping a selected organism,

comprising the steps of (a) combining tagged nucleic acid molecules with a selected target molecule under conditions and for a time sufficient to permit hybridization of the tagged molecules to the target molecule, wherein a tag is correlative with a particular fragment and is detected by non-fluorescent spectrometry or potentiometry, (b) separating the tagged fragments by sequential length or by size, (c) cleaving the tag from the tagged fragment, and (d) detecting the tag by non-fluorescent spectrometry or potentiometry, and therefrom determining the genotype of the organism (see columns 2-4 and 54). Since Ness *et al.*, teach combining tagged nucleic acid molecules with a selected target molecule under conditions and for a time sufficient to permit hybridization of the tagged molecules to the target molecule and separating the tagged nucleic acid molecules by sequential length (see columns 2, 3, and 54), the tagged nucleic acid molecules taught by Ness *et al.*, are with different mass. Therefore, Ness *et al.*, disclose hybridization of nucleic acid molecules to a set of probes of different nucleobase sequences, wherein each probe has a mass that differs from the one of all the other probes as recited in step (a) of claim 20. Since Ness *et al.*, teach that the nucleic acid molecules (ie., a DNA population which is covalently immobilized to the solid support and generated from mRNA) are immobilized at a surface of a support before step (a) (see column 54, lines 30-67) wherein the amines on the polymers of the solid support (ie., glass surface) are used to covalently immobilize oligonucleotides (see column 55, lines 9-67), and it is known that glass surface is a surface of the supports with a silicate or silane, Ness *et al.*, disclose the immobilization of the nucleic acid molecules at the surface is carried out via NH_2 as recited in step (b) of claim 20. Since Ness *et al.*, teach separating the tagged nucleic acid molecules by sequential length or separating the target molecules, hybridized tagged probes, unhybridized probes or target molecules,

probe:target hybrids, or tagged nucleic acid probes or molecules from other molecules utilizing methods which discriminate between the size of molecules such as HPLC or size exclusion chromatography (see columns 2-4 and 54) and it is known that HPLC or size exclusion chromatography is performed in a solvent, Ness *et al.*, disclose separation of the probes that are not hybridized and detachment of the probes that are hybridized in a solvent as recited in steps (c) and (d) of claim 20. Since Ness *et al.*, teach cleaving the tag from the separated tagged nucleic acid molecule, and detecting the tag by non-fluorescent spectrometry or potentiometry (see columns 2-4 and 54) such as electrospray ionization mass spectrometry (see column 3, last paragraph), Ness *et al.*, disclose analysis of the probes that are detached from step (d) by means of electrospray mass spectrometry as recited in step (e) of claim 20. Since, as shown above, Ness *et al.*, teach steps (a) to (e) for genotyping a selected organism, Ness *et al.*, disclose detecting the nucleotide sequence in the nucleic acid molecules by means of the probes hybridized to the nucleotide sequence as recited in step (f) of claim 20.

Therefore, Ness *et al.*, teach all limitation recited in claims 1-3, 6-10, 14, 16, 17, 19, and 20.

Response to Arguments

In page 11, last paragraph bridging to page 13, first paragraph of applicant's remarks, applicant argues that: (1) "[T]he main claim of the present invention relates to a method wherein the probes being used each have a distinct individual mass. The novel feature is not disclosed or suggested by the Ness reference."; (2) "[A]pplicant recognizes that dependent claims 6 and 8 further specify that the probe carry a tag. However, there is no disclosure, suggestion or teaching in the Ness reference to exclude or eliminate the step of cleaving the tags from the

probes, nor of the complete omission of the tags. On the other hand, the skilled artisan, after reading the present Specification, would conclude that the method according to the present invention does not extend to the mass spectrometrical Analysis of tags, but instead relates to the mass spectrometrical analysis of nucleic acid[s the] probes according to the invention consist of. See step (d) of claim 1 and page 5 of the Specification"; and (3) "the hybridization probes and the substances subjected to mass spectrometrical analysis are identical. This is simply not taught by Ness";

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, since Ness *et al.*, teach separating the tagged fragments (ie., probes) by sequential length or by size (see columns 2-4 and 54), Ness *et al.*, disclose that each probe has a distinct individual mass. Second, since the mass spectrometrical Analysis of tags taught by Ness *et al.*, is one of ways to analyze nucleic acid probes, Ness *et al.*, teach the rejected claims. Third, the rejected claims do not require that the hybridization probes and the substances subjected to mass spectrometrical analysis are identical as suggested by applicant. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ness *et al.*, (1997) as applied to claims 1-3, 6-10, 14, 16, 17, 19, and 20 above, and further in view of Shuber (US Patent No. 5,888,778, filed on June 16, 1997).

The teachings of Ness *et al.*, have been summarized previously, *supra.*

Ness *et al.*, do not disclose that the protein-substrate interaction is by means of an antibody-antigen bond as recited in claim 4.

Shuber teaches that antibodies is used to attach target nucleic acids to a solid support by coating the surfaces of the support with the antibodies and incorporating an antibody-specific hapten into the target nucleic acids. Alternatively, the target nucleic acids are attached directly to a solid support by epoxide/amine coupling chemistry (see column 11, second paragraph).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have immobilized the nucleic acid molecules recited in claim 1 by means of an antibody-antigen bond in view of the patents of Ness *et al.*, and Shuber. One having ordinary skill in the art would have been motivated to do so because Shuber has successfully attached target nucleic acids to a solid support by coating the surfaces of the support

with the antibodies and incorporating an antibody-specific hapten into the target nucleic acids and the simple replacement of one well known immobilization method (i.e., amine coupling chemistry taught by Ness *et al.,*) from another well known immobilization method (i.e., antibody-antigen bond taught by Shuber) during the process of performing the method recited in claim 1 would have been, in the absence of convincing evidence to the contrary, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made because immobilization by amine coupling taught by Ness *et al.,* and immobilization by antibody-antigen bond taught by Shuber are two functional equivalent methods for nucleic acid immobilization which are used for the same purpose and two methods are exchangeable (see Shuber, column 11).

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.06.

10. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ness *et al.,* (1997) further in view of Shuber (US Patent No. 5,888,778, filed on June 16, 1997) a applied to claims 1-4, 6-10, 14, 16, 17, 19, and 20 above, and further in view of Cros *et al.,* (US Patent No. 5,849, 480, 102 (e) date: March 16, 1995).

The teachings of Ness *et al.,* and Shuber have been summarized previously, *supra.*

Ness *et al.,* and Shuber do not disclose that the protein-nucleic acid interaction is by means of a Gene32-nucleic acid bond as recited in claim 5.

Cros *et al.*, teach to attach a nucleic acid fragment-hapten conjugate onto the solid support by interacting with an anti-conjugate compound such as Gene32 protein coated on the support. The anti-conjugate compound can be an anti-nucleic acid fragment antibody (see column 5, lines 7-39).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have immobilized the nucleic acid molecules recited in claim 1 by means of a Gene-32 protein-nucleic acid bond in view of the patents of Ness *et al.*, and Cros *et al.*. One having ordinary skill in the art would have been motivated to do so because Cros *et al.*, has successfully attached a nucleic acid fragment-hapten conjugate onto the solid support by interacting with an anti-conjugate compound (ie., Gene32 protein) coated on the support and Gene32 protein coated on the support would reduce non-specific binding of the nucleic acid fragment to the support because this protein only binds to single stranded nucleic acids (see column 5, lines 21-39), and the simple replacement of one known immobilization method (i.e., anti-nucleic acid fragment antibody-nucleic acid bond taught by Shuber) from another well known immobilization method (i.e., Gene-32 protein-nucleic acid bond taught by Cros *et al.*,) during the process of performing the method recited in claim 1 would have been, in the absence of convincing evidence to the contrary, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made because immobilization of the nucleic acid by anti-nucleic acid fragment antibody-nucleic acid bond taught by Shuber and immobilization of the nucleic acid by Gene-32 protein-nucleic acid bond taught by Cros *et al.*, are two functional equivalent methods which are used for the same purpose, and both anti-nucleic acid fragment

antibody and Gene-32 protein are anti-conjugate compound and are exchangeable (see Cros *et al.,* column 5, lines 21-39).

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.06.

11. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ness *et al.,* as applied to claims 1-3, 6-10, 14, 16, 17, 19, and 20 in view of Cook *et al.,* (US Patent No. 5,614,617, 102 (e) date: February 18, 1993).

The teachings of Ness *et al.,* have been summarized previously, *supra.*

Ness *et al.,* do not disclose that the probes are modified by introducing a phosphorothioate group, a RNA base, a phosphotriester bond or a combination thereof into the probe as recited in claim 15.

Cook *et al.,* teach that the modified base in the nucleic acid includes substitution of amine group for an oxygen and the modification of the sugar phosphate nucleic acid backbone by phosphorothioate or phosphotriester moiety (see column 8, second paragraph).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claim 15 wherein the probes are modified by introducing a phosphorothioate group, a RNA base, a phosphotriester bond or a combination thereof into the probe as recited in claim 15 in view of the patents of Ness *et al.,* and Cook *et al.*. One having ordinary skill in the art would have been motivated to

do so because Ness *et al.*, state that "[F]rom the foregoing, it will be appreciated that, although specific embodiments of the invention have been described herein for purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention" (see column 118, right column) and the simple replacement of one modified base (ie., modified an oxygen by substitution of amine) from another modified base (ie., the modification of the sugar phosphate nucleic acid backbone by phosphorothioate or phosphotriester moiety) during the process of performing the method recited in claim 15 would have been, in the absence of convincing evidence to the contrary, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made because these modified bases are exchangeable.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.06 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

12. Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ness *et al.*, as applied to claims 1-3, 6-10, 14, 16, 17, 19, and 20 in view of Stratagene catalog (page 39, 1998).

The teachings of Ness *et al.*, have been summarized previously, *supra.*

Regarding claim 18, since, as shown the rejection under 35 U.S.C 102, Ness *et al.*, teach claim 6, Ness *et al.*, disclose a set of probes as defined in claim 6 as recited in (a) of claim 18. Since Ness *et al.*, teach a solid support coated with an amine-polymer wherein the amines on the polymer are used to covalently immobilize oligonucleotides (see column 55, lines 9-67), Ness *et al.*, disclose a probe support which has been pretreated and thus allows for the attachment of target DNAs as recited in (b) of claim 18.

Ness *et al.*, also teach a kit comprising a plurality of amplification primer pairs (see column 41, lines 61-67 and column 42, lines 1-13).

Stratagene catalog teaches a motivation to combine reagents into kit format (page 39).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine a set of probes and a probe support taught by Ness *et al.*, into a kit format as discussed by Stratagene catalog since the Stratagene catalog teaches a motivation for combining reagents of use in an assay into a kit, "[E]ach kit provides two services: 1) a variety of different reagents have been assembled and pre-mixed specifically for a defined set of experiments. 2) The other service provided in a kit is quality control" (page 39, column 1).

Response to Arguments

In page 13, first paragraph of applicant's remarks, applicant argues that: "[T]he secondary references fails to remedy the deficiencies of Ness. None of the cited prior art references, either singly or in combination, disclose or suggest the present invention".

This argument has been fully considered but it is not persuasive toward the

withdrawal of the rejection. First, the examiner has clearly indicated in the rejections under 35 U.S. C 103 (a) why the claims 4, 5, and 18 are rejected. Second, applicant does not explain why either singly or in combination of these references does not disclose or suggest the present invention.

Conclusion

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. No claim is allowed.

14. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30

(November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703)872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571)272-0745.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

Frank Lu
PSA
October 22, 2004

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